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02/28/90

☒ This application has been examined ☒ Responsive to communication filed on Jan. 8, 1990 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire three(3) month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892. 2pp 2. ☒ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449. 4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474. 6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-16 are pending in the application.
Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-16 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received
☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

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EXAMINER'S ACTION

The application should be reviewed for errors.

Claims 4 and 5 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4, line 2,
5 recites "for" which appears to be a typographical error. Correction or further clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

10 "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

15 The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention. Table I (page 20) shows only a percentage of the transformants were "killers" to any extent. It is not clear if this is because the plants were not transformed or because the expression of the toxin was so low as to be non-detectable.

20 Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

25 "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject
30 matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5 Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person."

10 This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

15 Claims 1-16 are rejected under 35 U.S.C. 103 as being unpatentable over Hoekma et al taken with Murray et al, Schnepf et al, Vaeck et al, Hollenberg et al, and Seeburg et al. Hoekma et al teaches a method of affecting gene expression by exploiting the codon usage. Hoekma et al disclose that when foreign proteins are used in yeast vector systems the
20 expression level may decrease one or two orders of magnitude. Hoekma et al teach that the codon choice pattern was one parameter affecting this low level of expression and teaches that expression of native highly expressed yeast genes can be altered by substituting the codons usually found in yeast genes with minor codons which never or rarely occur in highly expressed
25 natural genes. The amino acid sequence was not disturbed. As a result, both mRNA and protein synthesis were decreased. Hoekma et al differs from the claimed invention primarily in that his work is directed to yeast cells, not plant cells as in the claimed invention. However, information on the codon usage in plants has been extensively reviewed. In a recent
30 review, Murray et al teach that plant genes in general were known to be highly GC rich, especially in the third base as compared to procaryotic

sequences which have a strong bias towards use of A or T in the third base. More specifically, in Bacillus thuringiensis as reported by Schnepf et al it was known that the use of A or T was preferred. Additionally, it was known that B. thuringiensis toxins in particular were poorly expressed in plant cells as reported for example by Vaeck et al. Furthermore, Murray et al suggested the modification of the primary nucleic acid structure based upon the codon usage to increase expression in plants. Thus, it would have been obvious to one of ordinary skill in the art that the concept taught by Hoekma et al to address the problem of poor expression of foreign genes in yeast could be applied to poor expression of foreign genes in plants.

Methods of transfer of foreign genes to plant cells and expression in plant cells are all well within the ordinary level of skill in the art. Methods of making long oligonucleotides are known in the art as taught by Hoekma et al Hollenberg et al (Figure 9) and Seeburg et al (Figure 2).

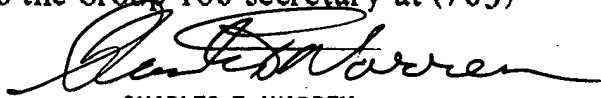
Consequently, the application of the teaching of Hoekma et al to expression of plant cells was well within the ordinary skill in the art at the time the claimed invention was made as adequately demonstrated by the secondary references. One of ordinary skill would have had a reasonable expectation of success in enhancing gene expression by substituting the codons employed by the native gene with codons used in the host cell in view of the teaching of the prior art. See In re O'Farrell, 7 USPQ2d 1673 at 1681 (Fed. Cir. 1988). Thus the claimed invention as a whole was clearly prima facie obvious over the references, in the absence of sufficient, clear, and convincing evidence to the contrary.

No claim is allowed.

An inquiry concerning this communication should be directed to Barbara M. Chereskin, Ph.D., at telephone number (703) 557-7721. Inquiries of a general nature should be directed to the Group 180 secretary at (703) 557-0664.

BMC

2/26/90


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